

This Page Is Inserted by IFW Operations  
and is not a part of the Official Record

## **BEST AVAILABLE IMAGES**

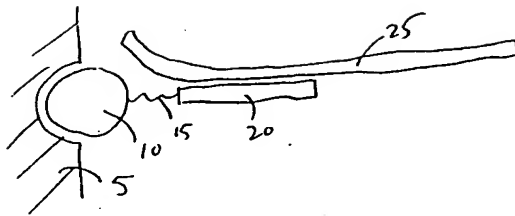
Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

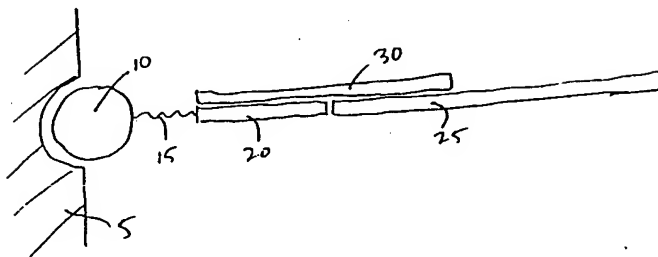
- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

**IMAGES ARE BEST AVAILABLE COPY.**

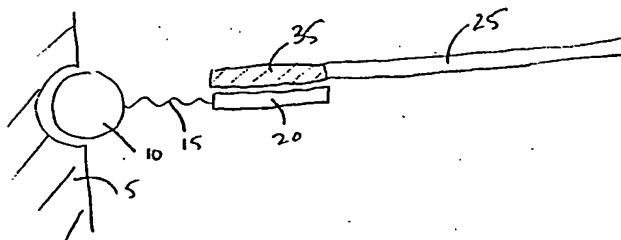
**As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.**



A



B



C

Fig 1

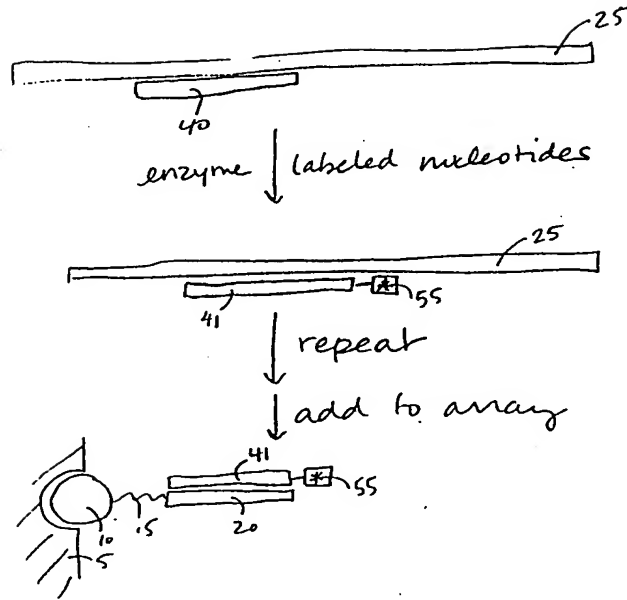


Fig 2A

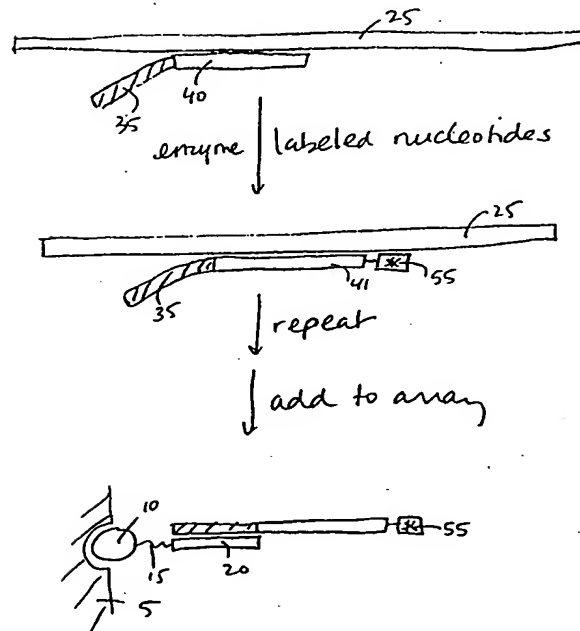


Fig 2B

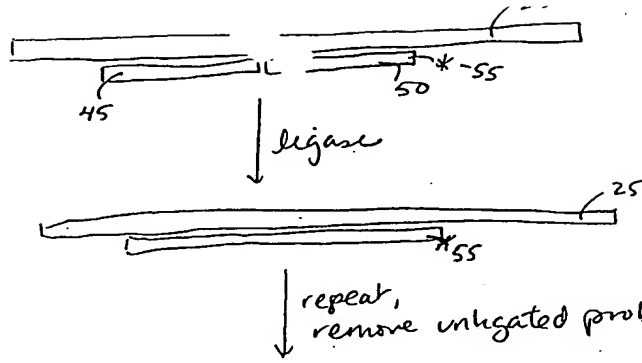


Fig 3A

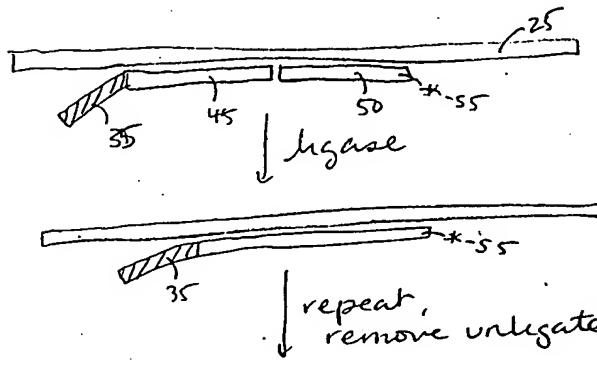
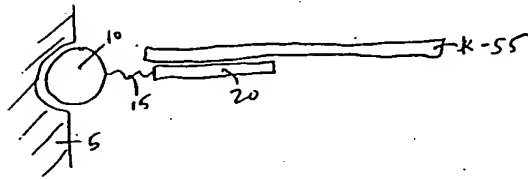
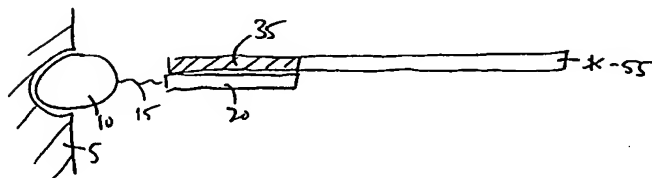


Fig 3B



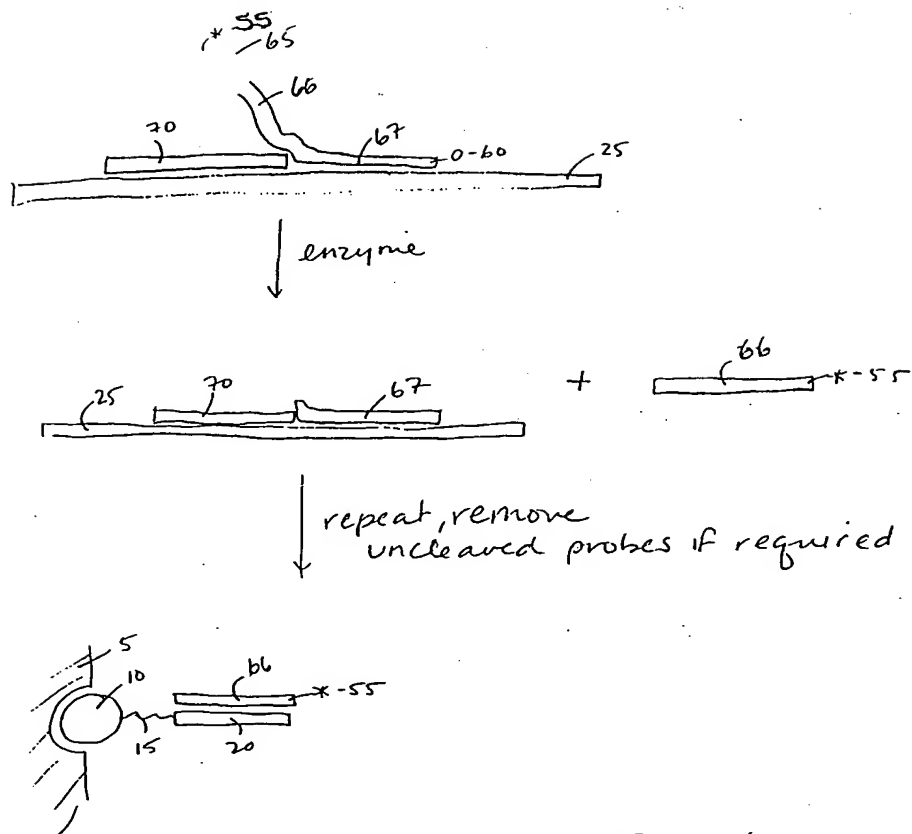


Fig 4

FIG 5A

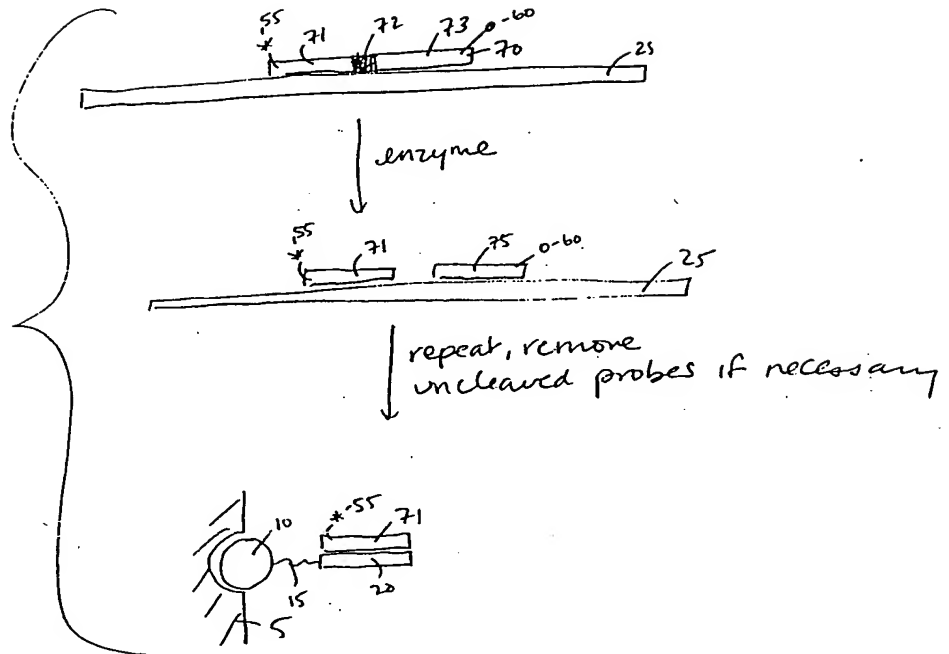
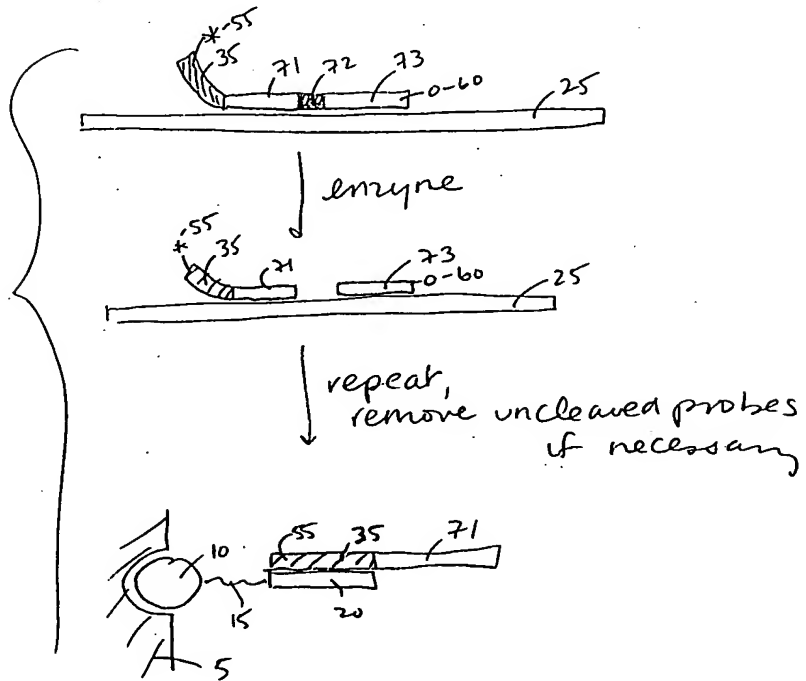


Fig 5B



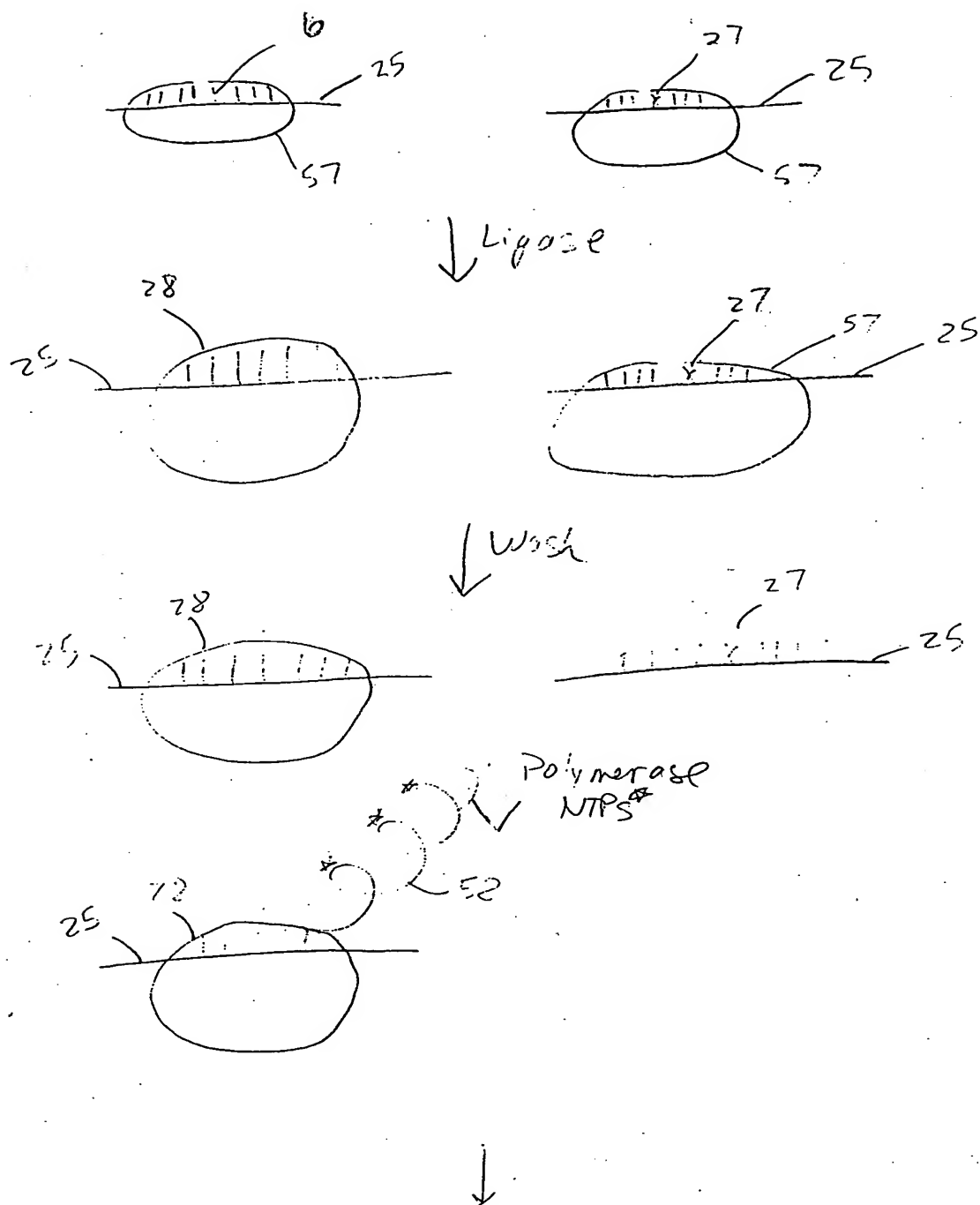


FIGURE 6



↓ Restriction  
Endonuclease

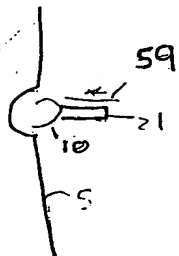
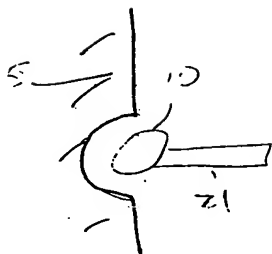
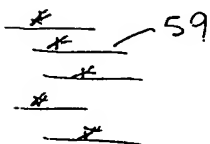
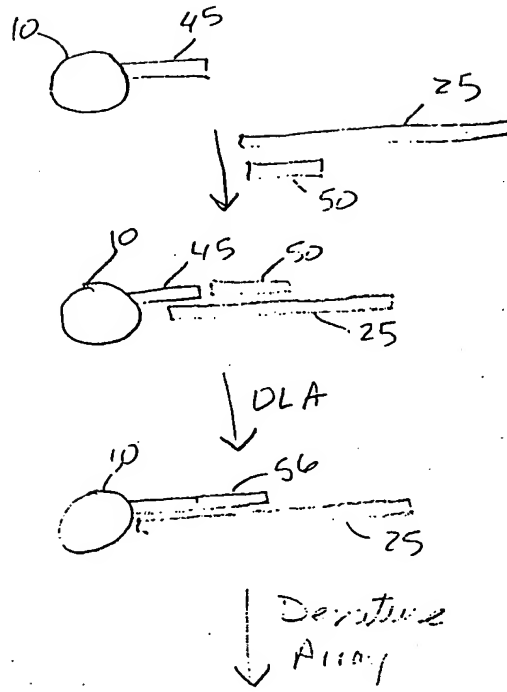


FIGURE 6  
Continued





A

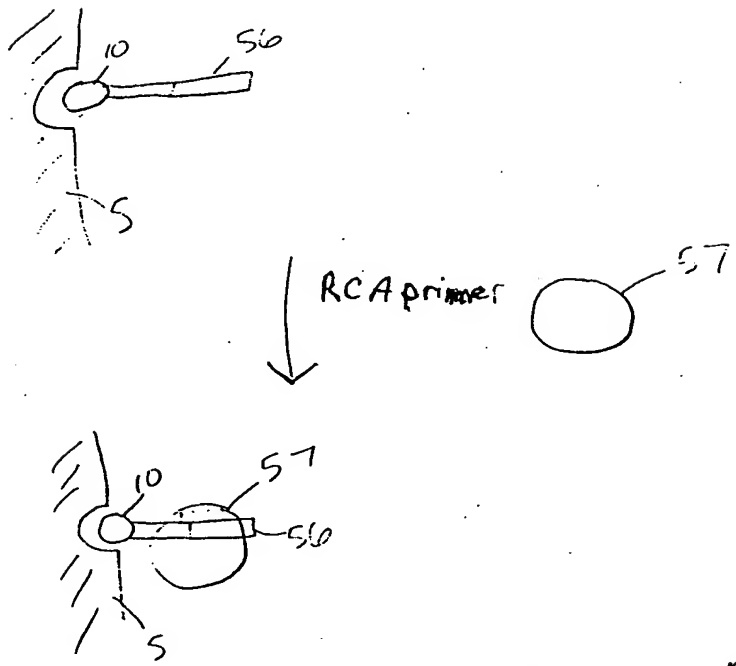


FIGURE 7

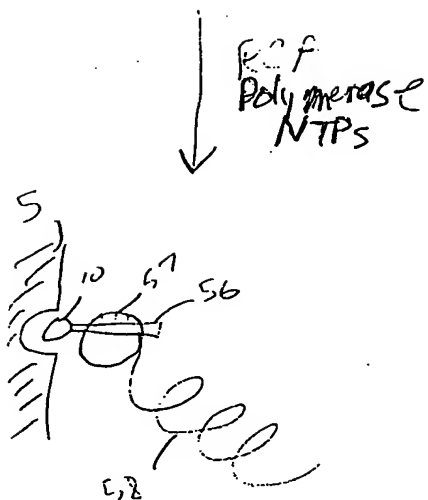


FIGURE 7  
(continued)

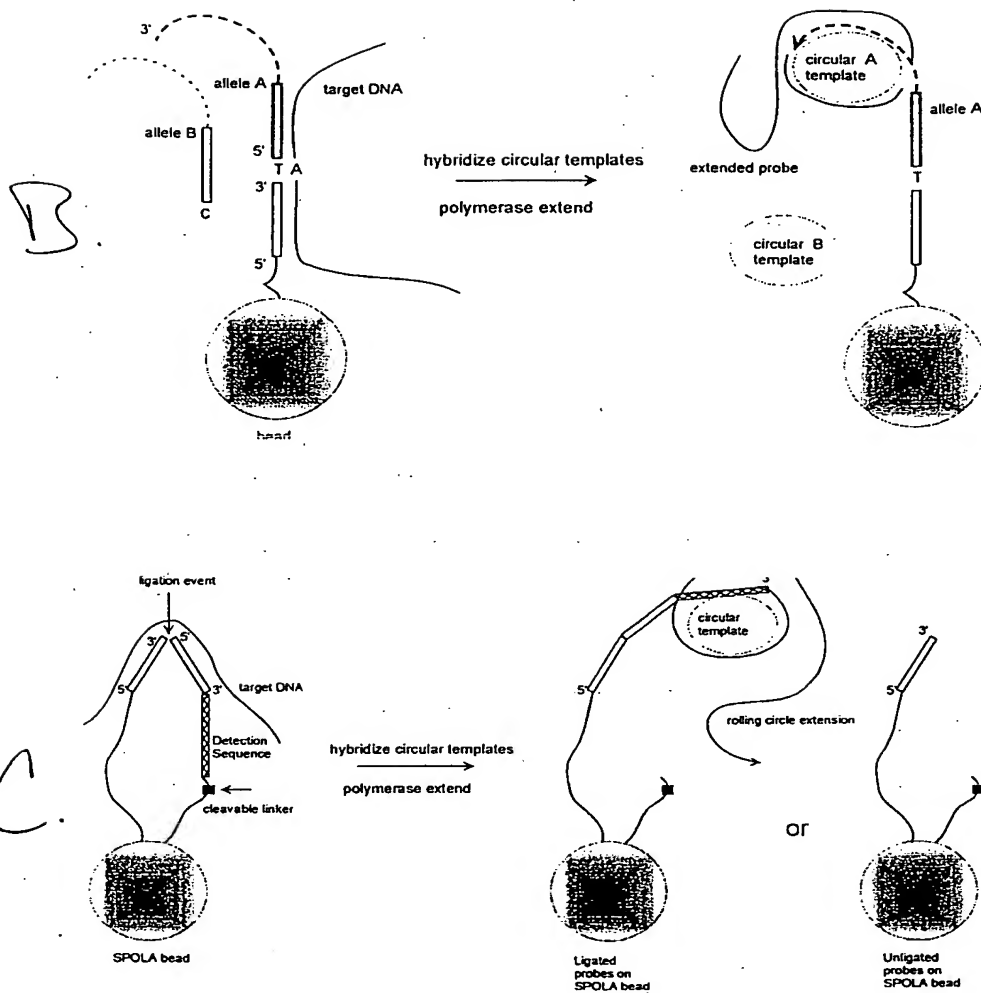


Figure 7 continued

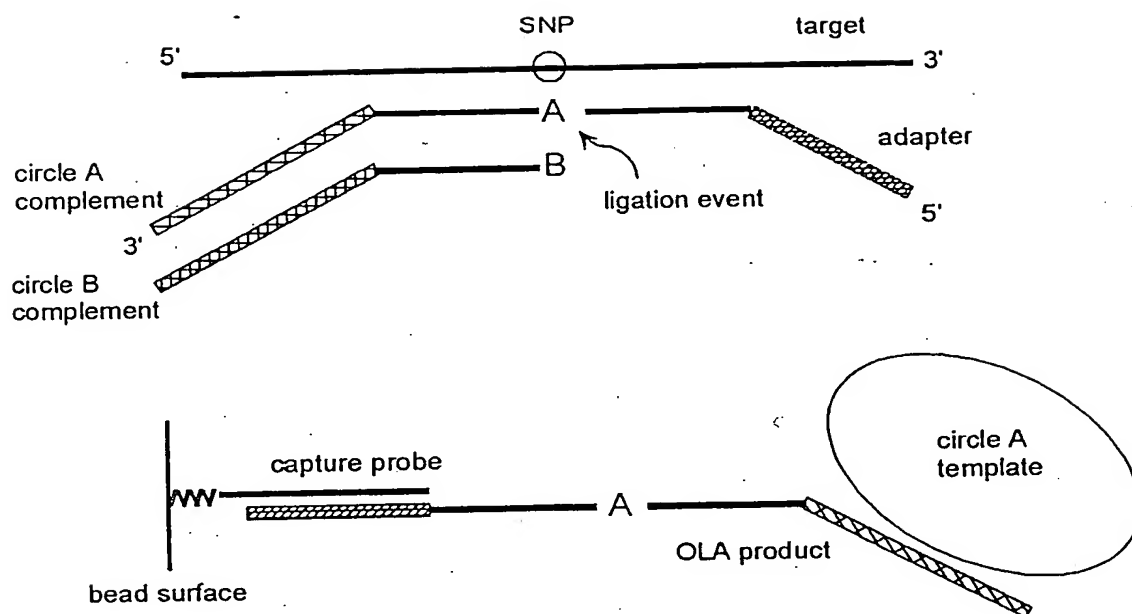
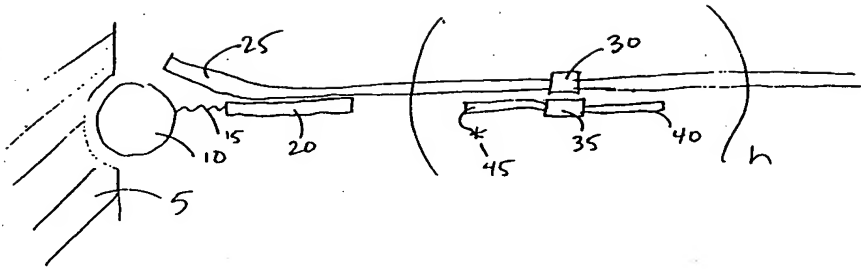
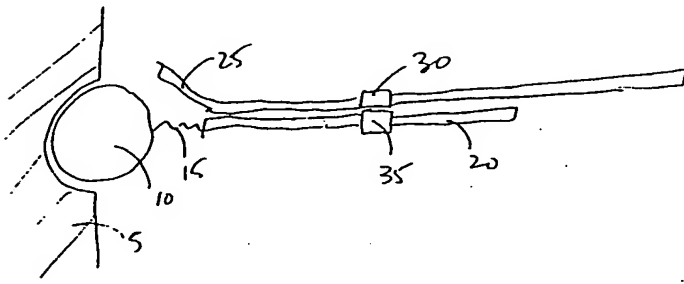


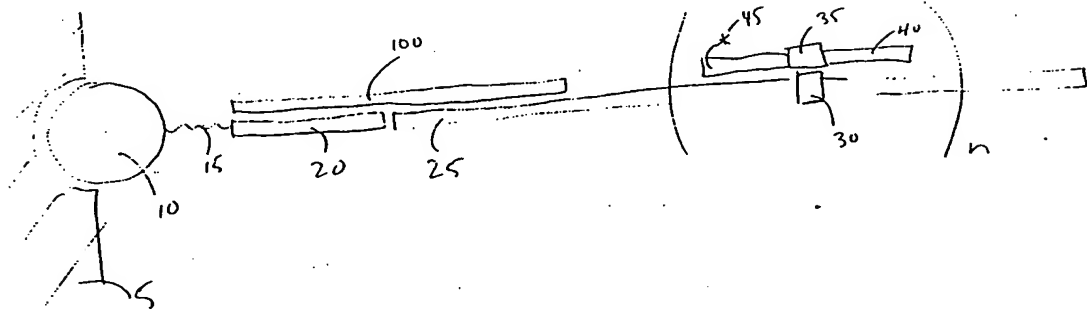
Figure 7 continued



A



B



C

FIGURE 8

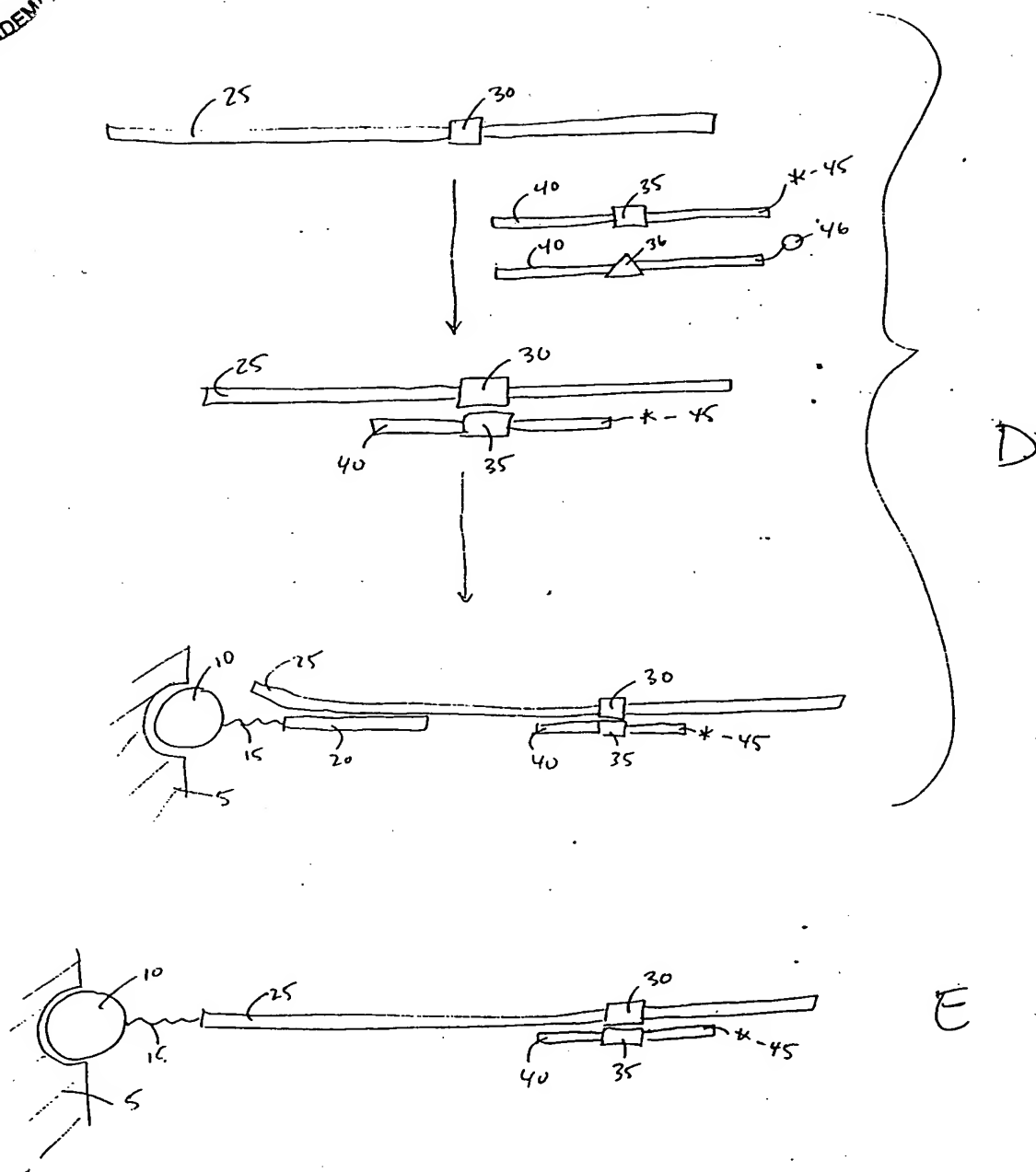
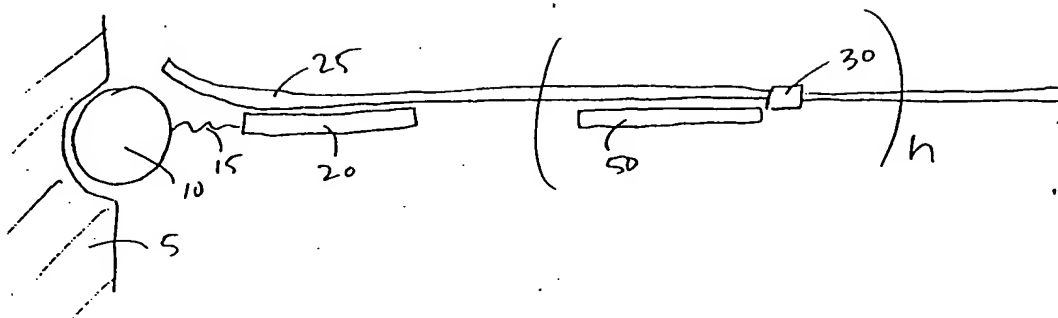
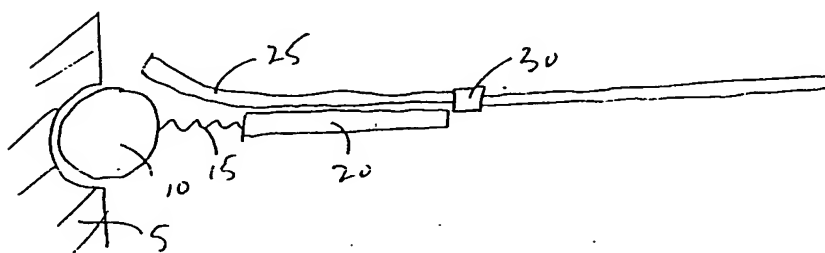


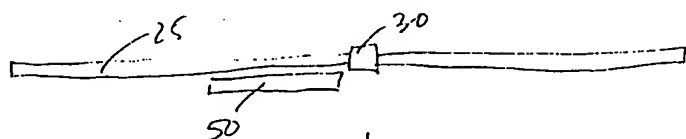
FIGURE 8  
(continued)



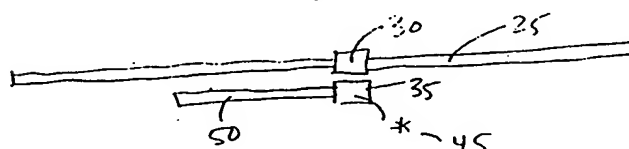
A



B



labelled NTP enzyme



optional removal of unextended primers

denature, add to array

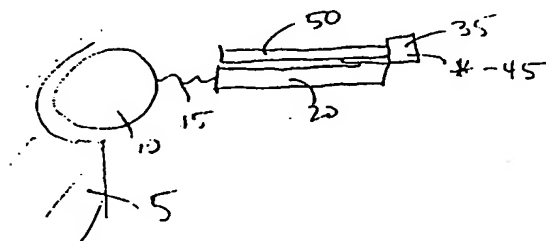


FIGURE 9.

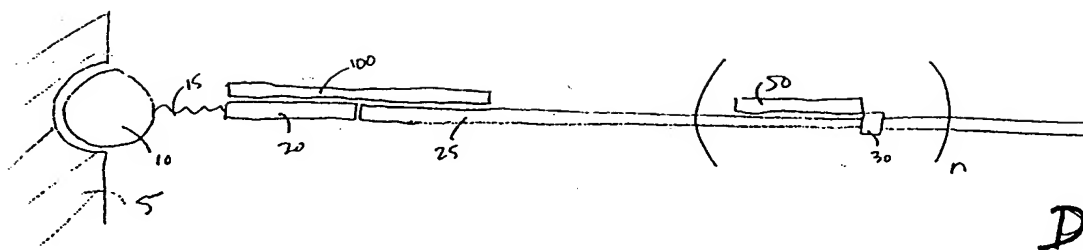
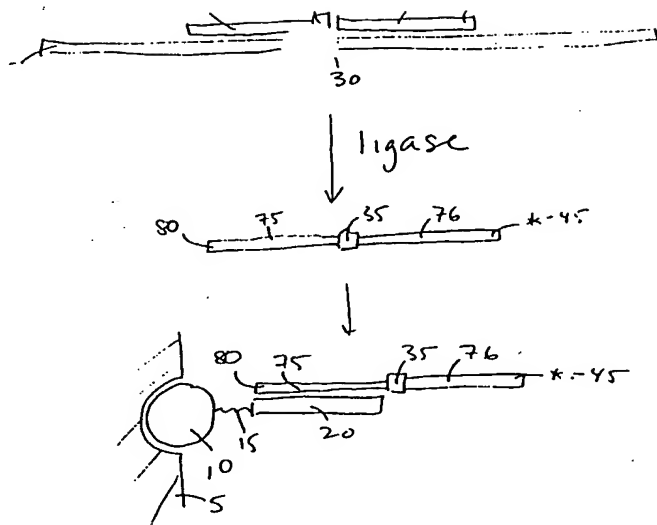
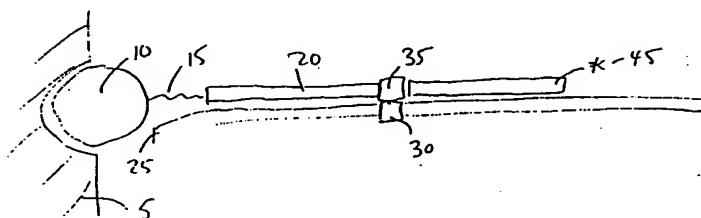


FIGURE 9  
(continued)

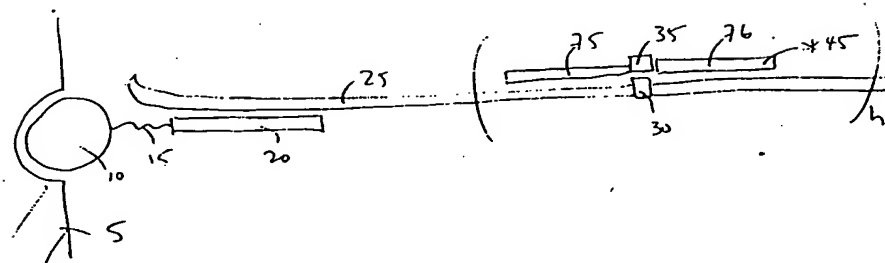




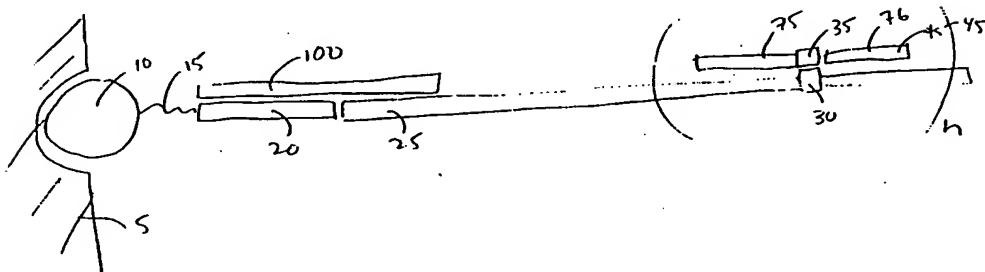
A



B



C

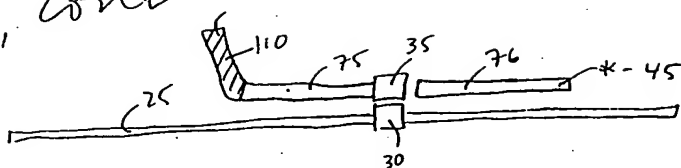


D

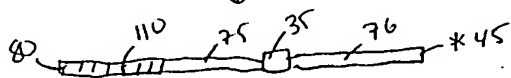
FIGURE 10.



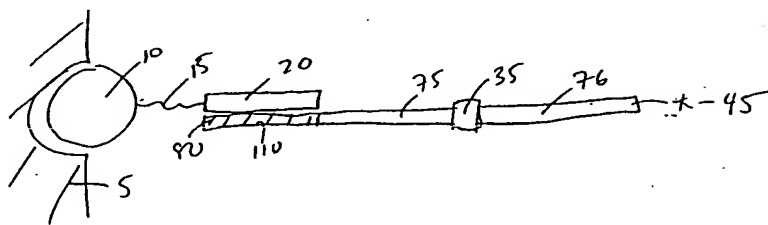
cont



ligate



to array



E

FIGURE 10  
(continued)

SPDLA Hsray

SPDLA Hsray

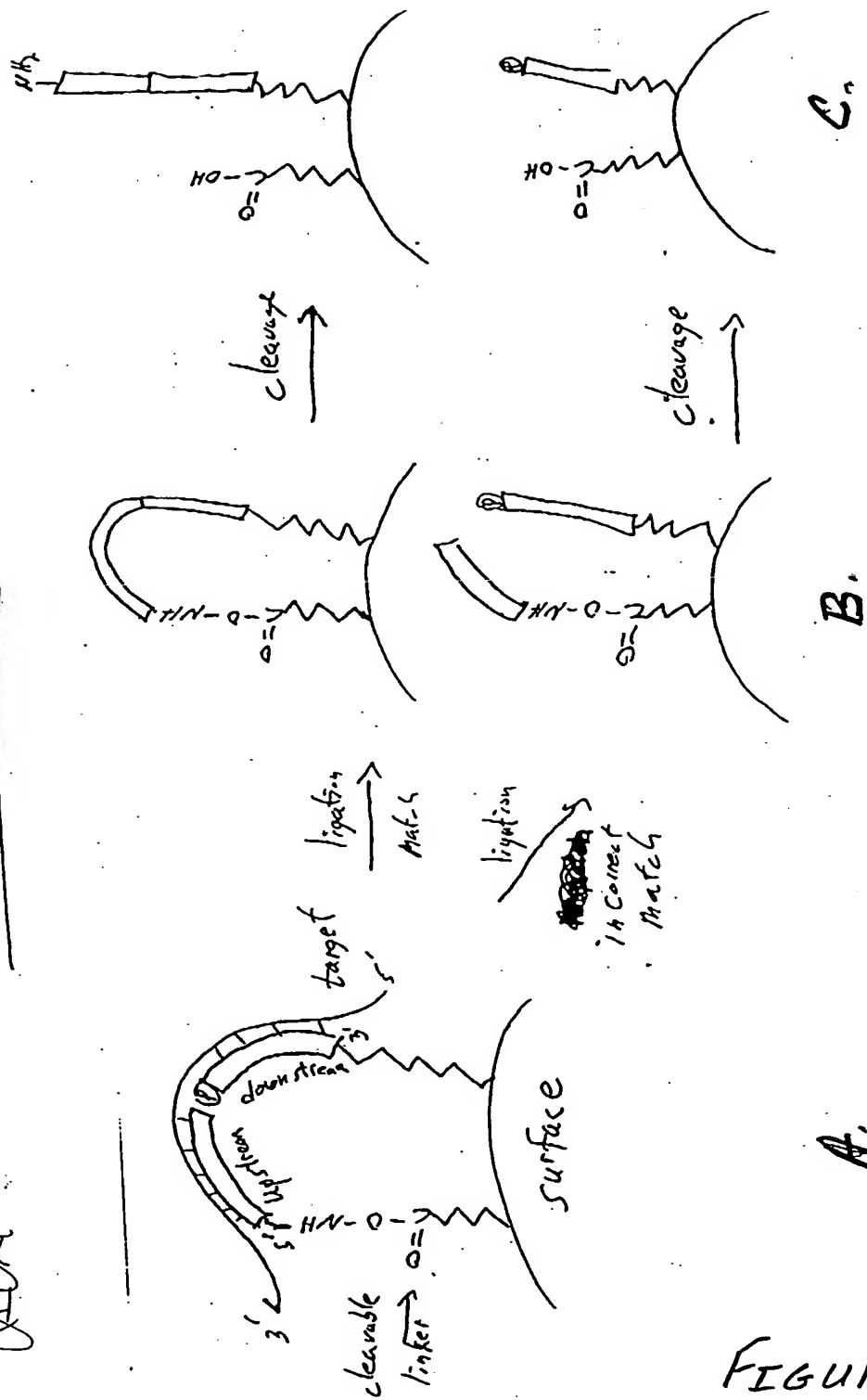


FIGURE 11

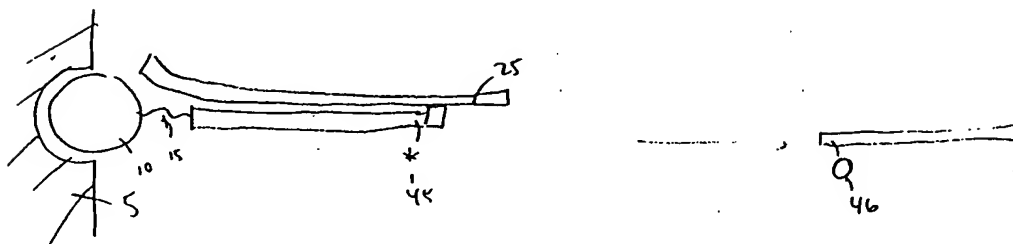
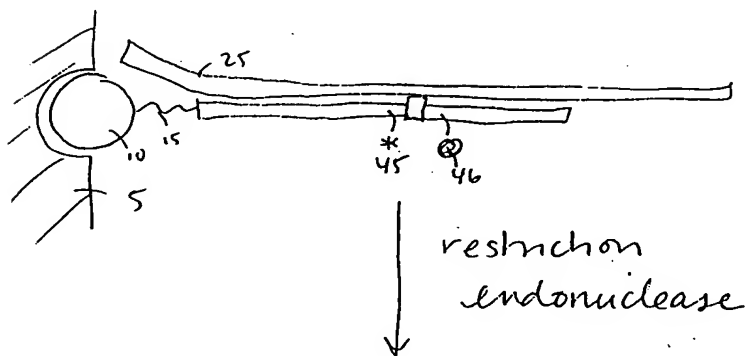
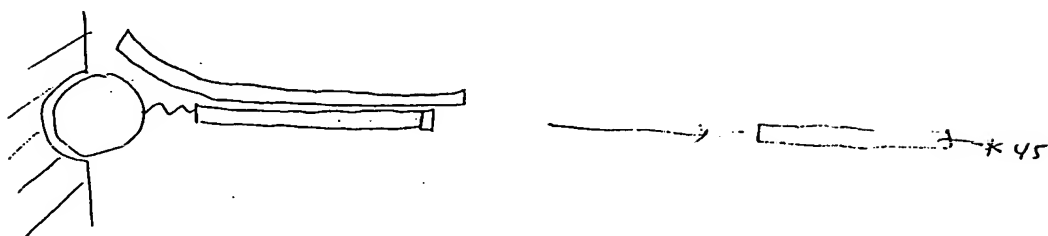
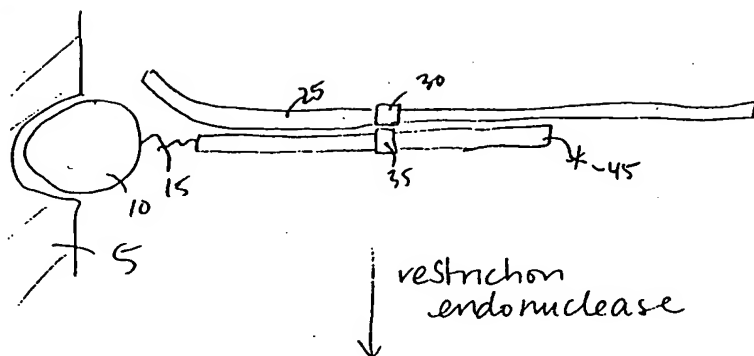
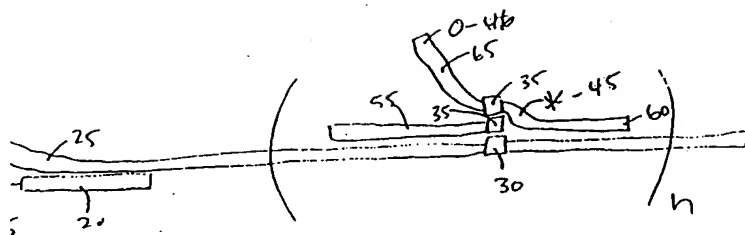
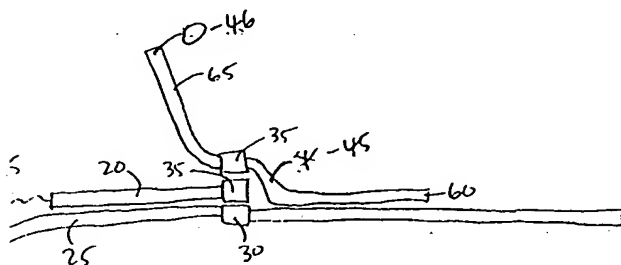


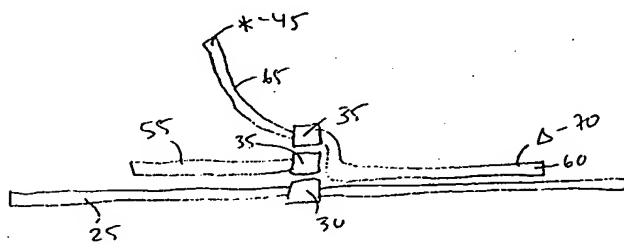
FIGURE 12



A

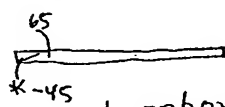


B



C

enzyme



optional remove undecayed signal probe, add to array

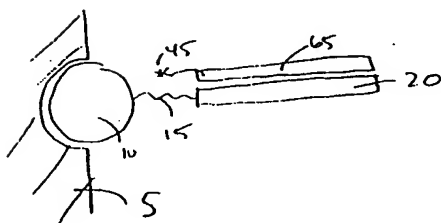
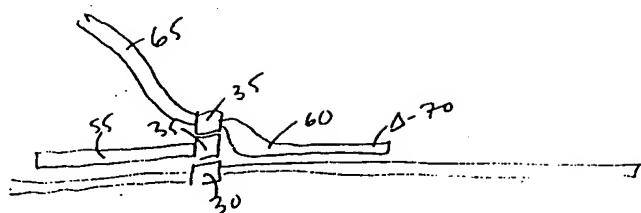
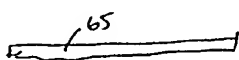


FIGURE 13



enzyme



optional removal of  
unreacted primers,  
optional ligase

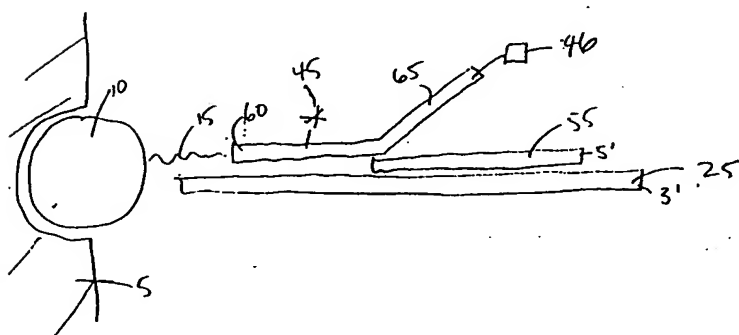
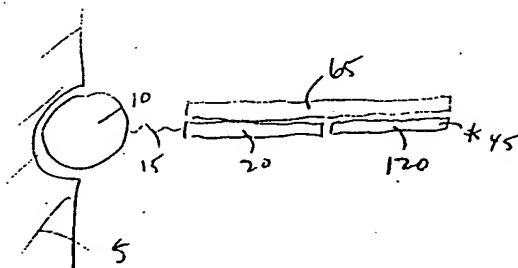
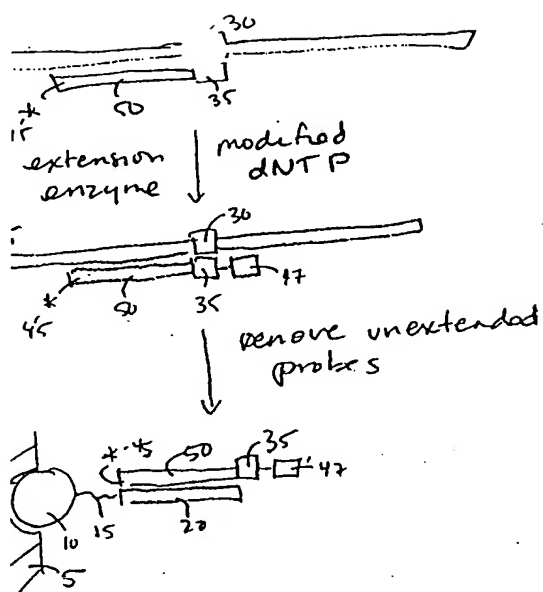
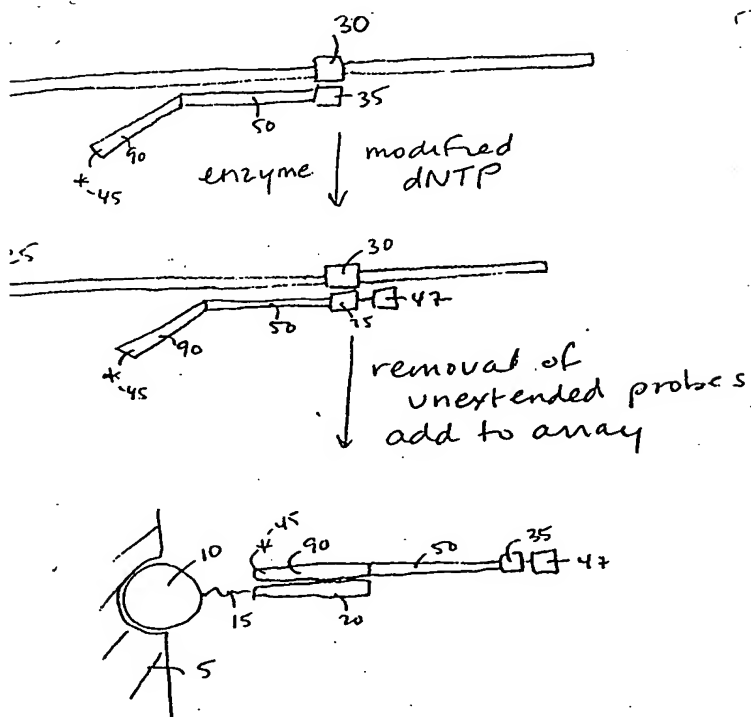


FIGURE 13  
 (continued)



A



B

FIGURE 14

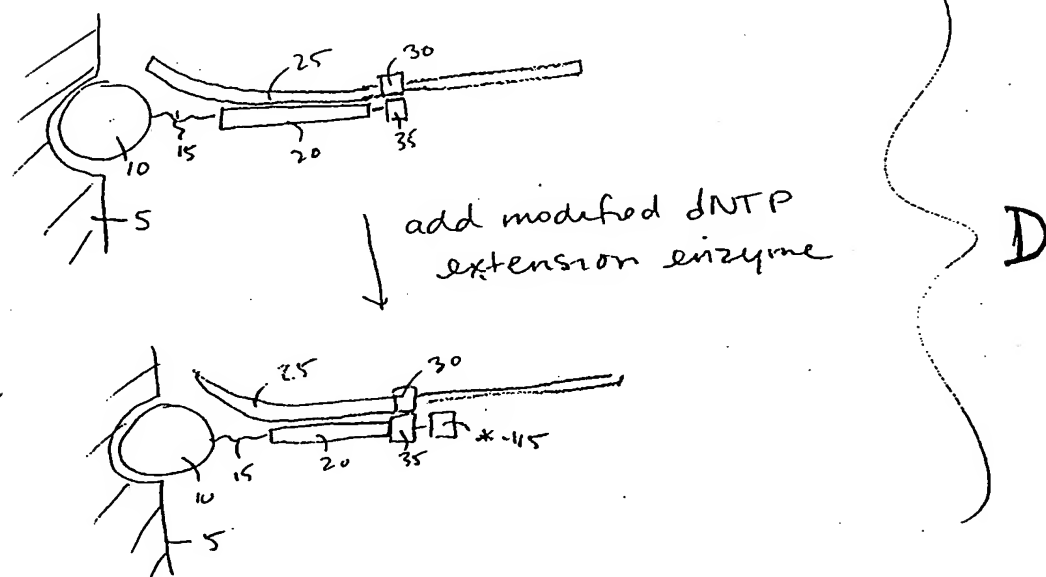
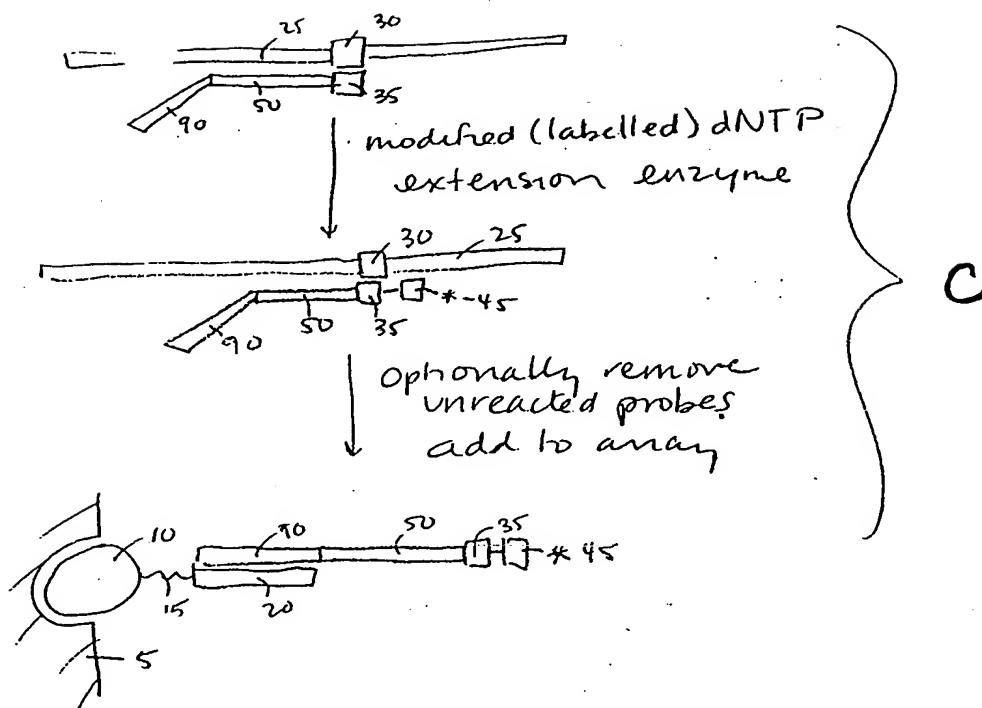


FIGURE 14 (continued)



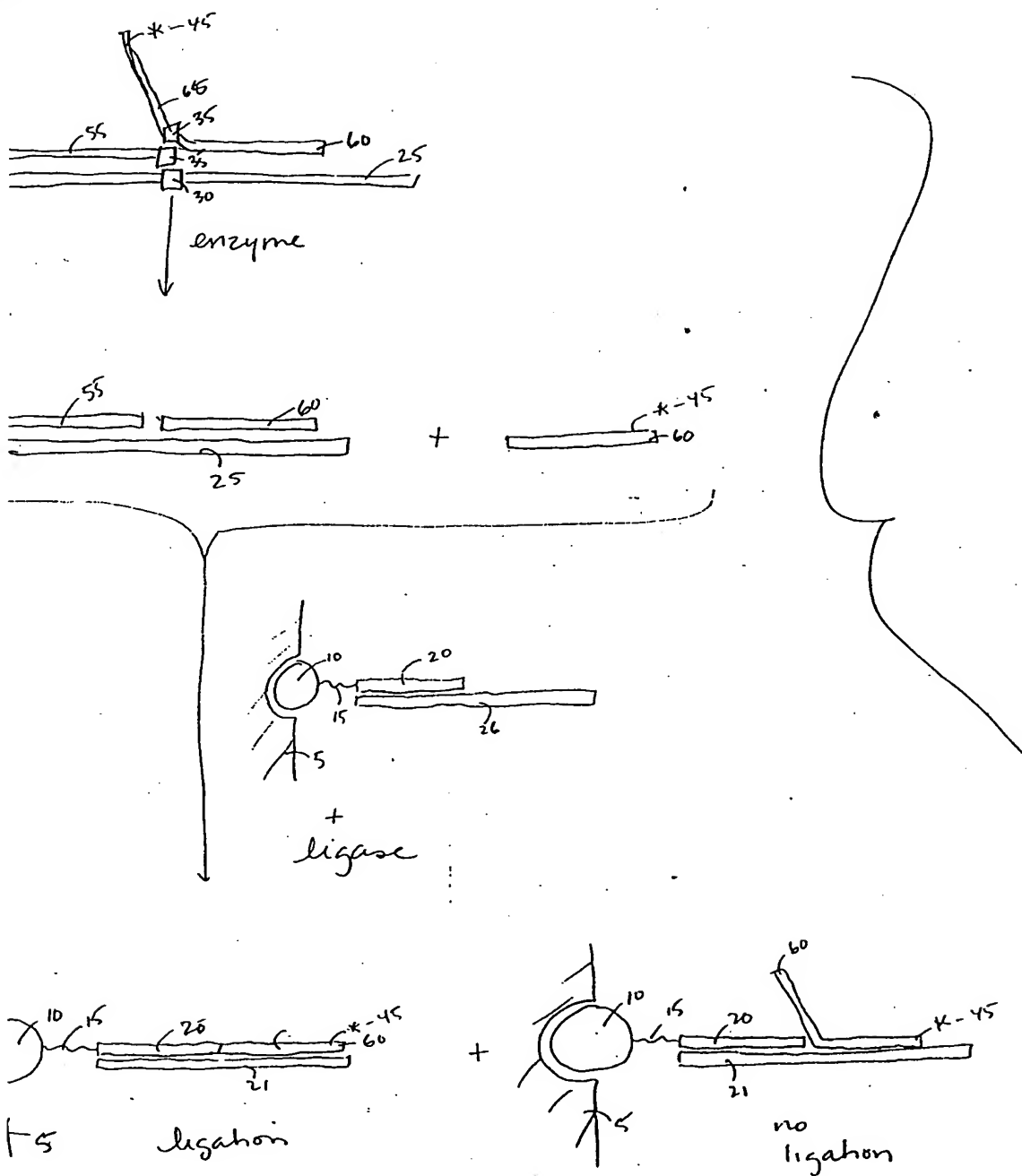
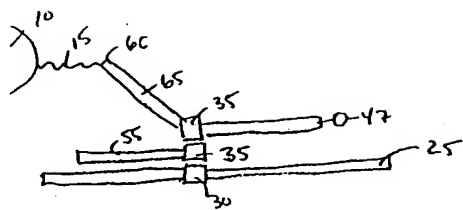
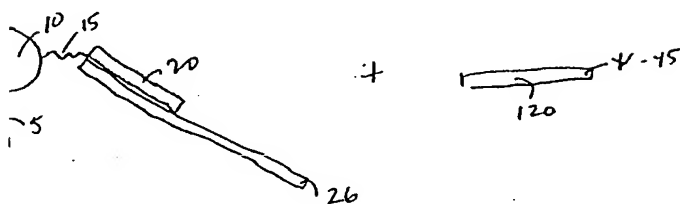


FIGURE 15A



↓ cleavage enzyme  
target template



↓ ligation

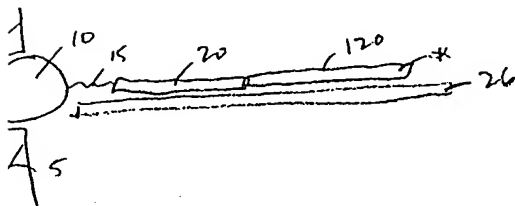


FIGURE 15B

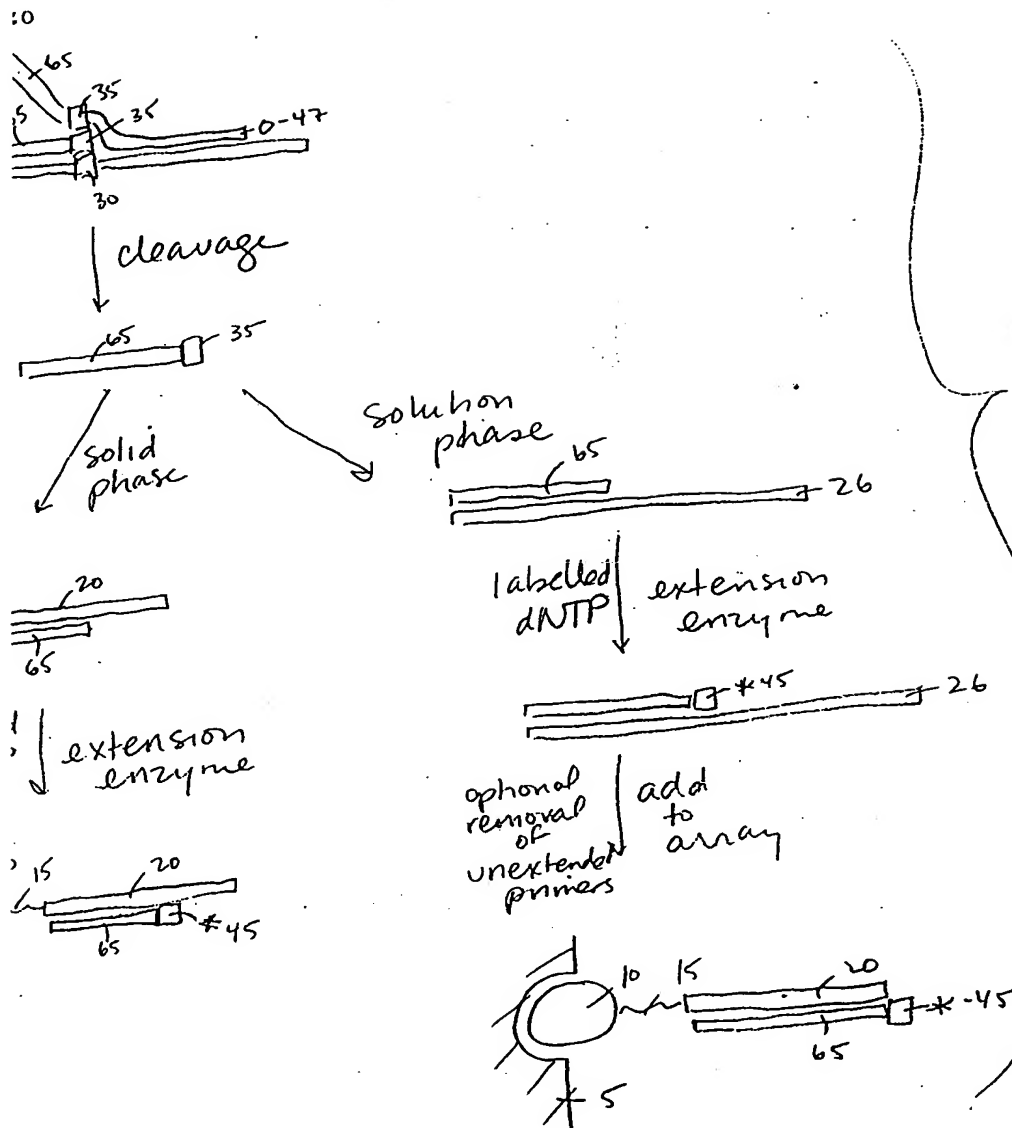


FIGURE 16A

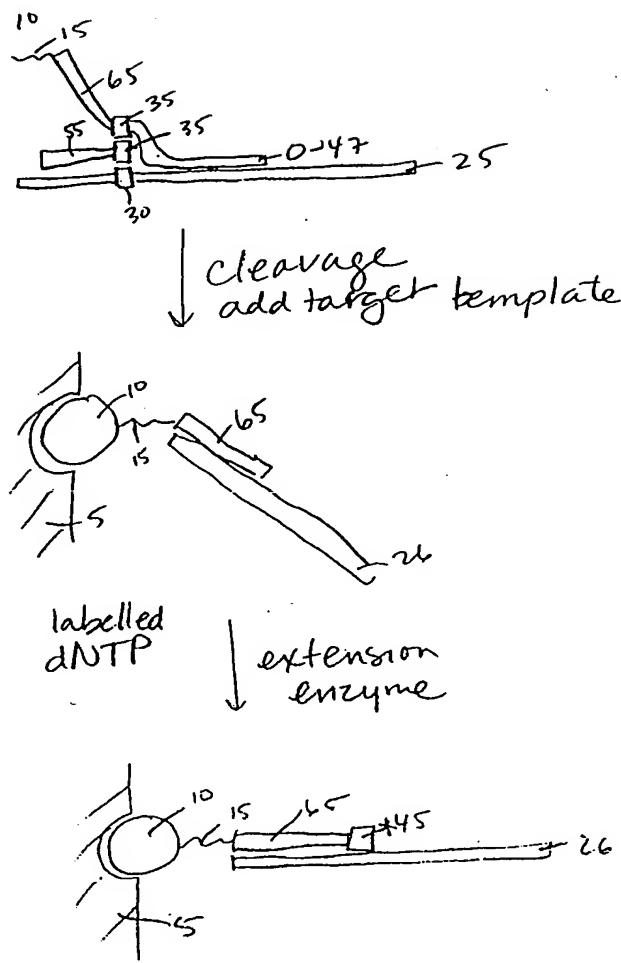


FIGURE 16 B

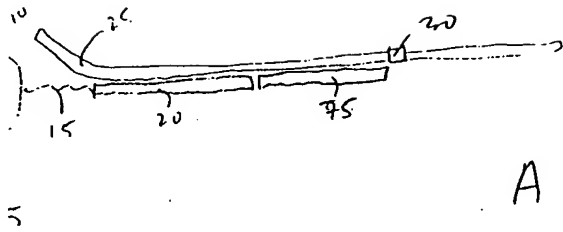
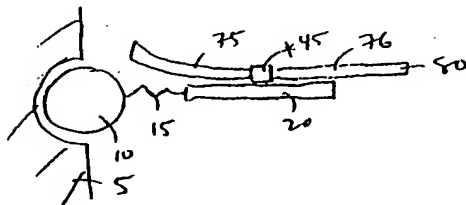
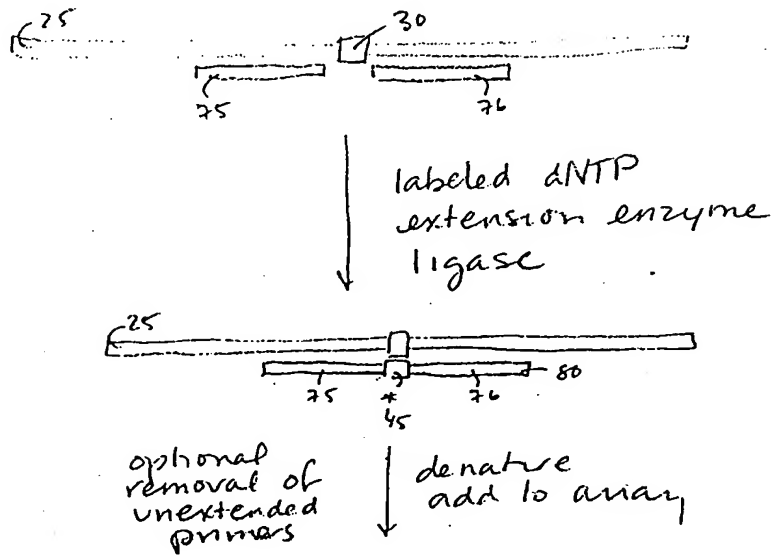
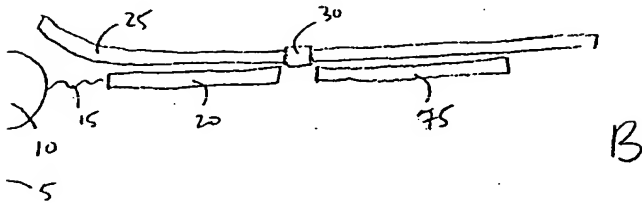


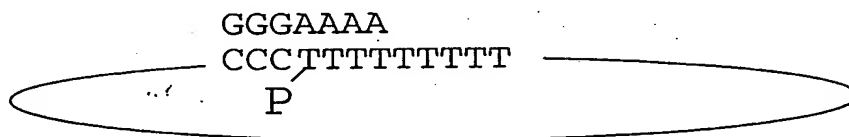
FIGURE 17



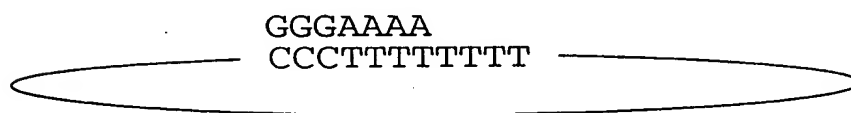


3'CCC ————— TTTTTTTT-P 5'  
cDNA

- (1) Circularize cDNA  
with guide linker



- (2) Ligate



- (3) Extend as  
Rolling circle

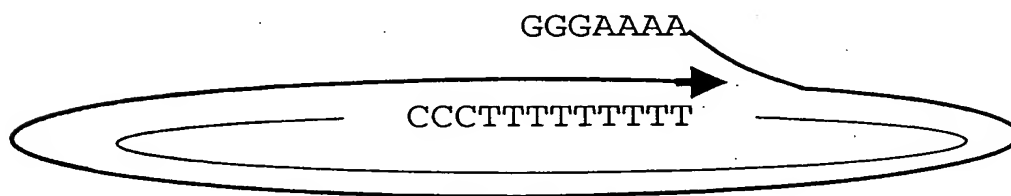
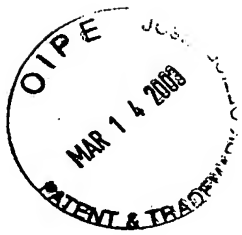


Figure 18



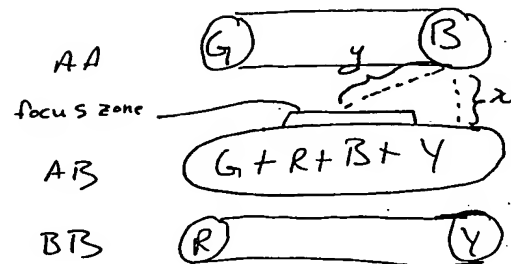
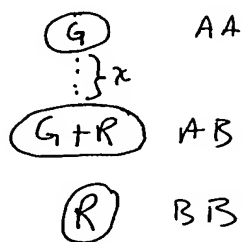
### Single Labeled Probe

Genotype	Signal
AA	G/G
AB	G/R
BB	R/R

### Multi-Labeled Probe

Genotype	Signal
AA	G <sub>1</sub> B / G <sub>2</sub> B
AB	G <sub>1</sub> B / R <sub>2</sub> Y
BB	R <sub>1</sub> Y / R <sub>2</sub> Y

### Signal Range



$x$  = single label distance  
 $y$  = multi label distance

Figure 19

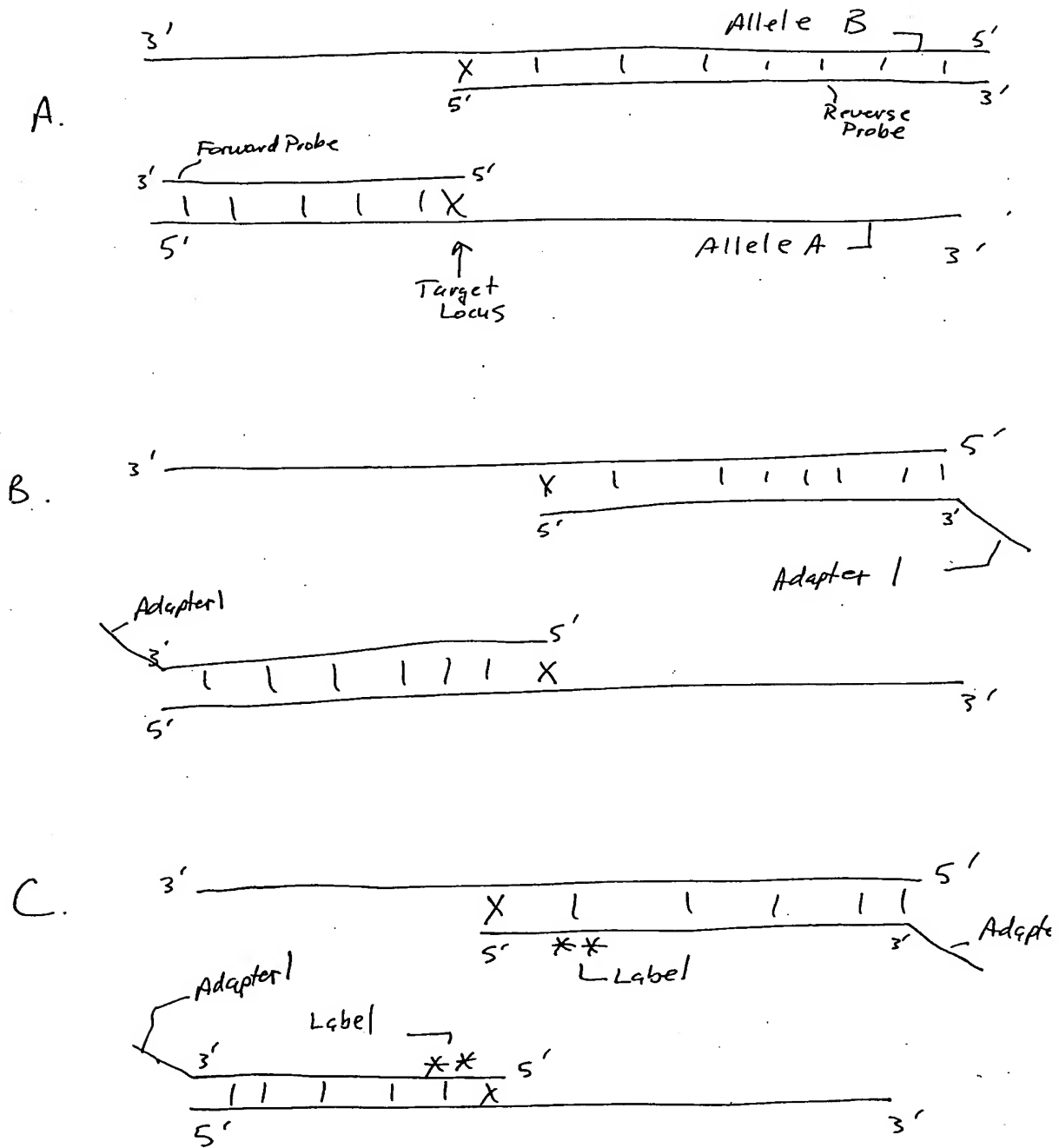


Figure 20



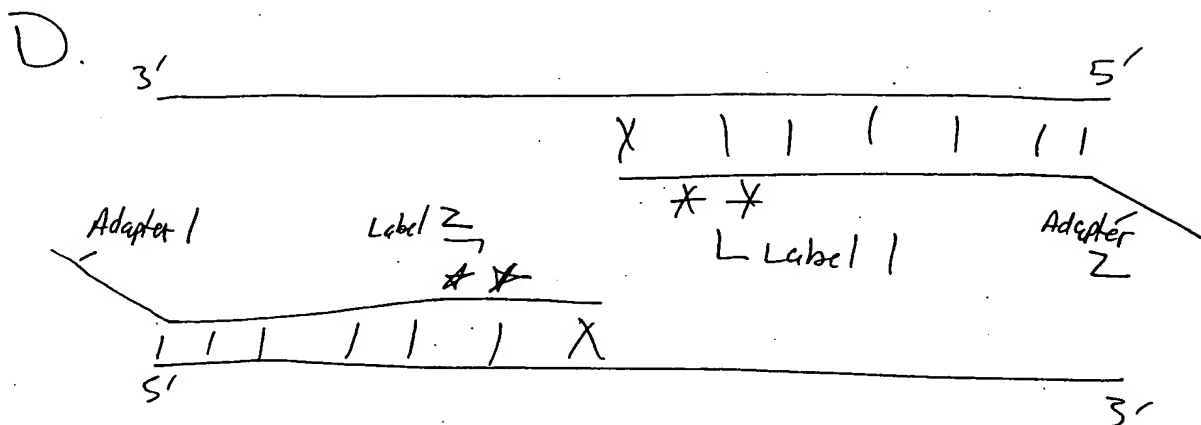


Figure 20 (continued)

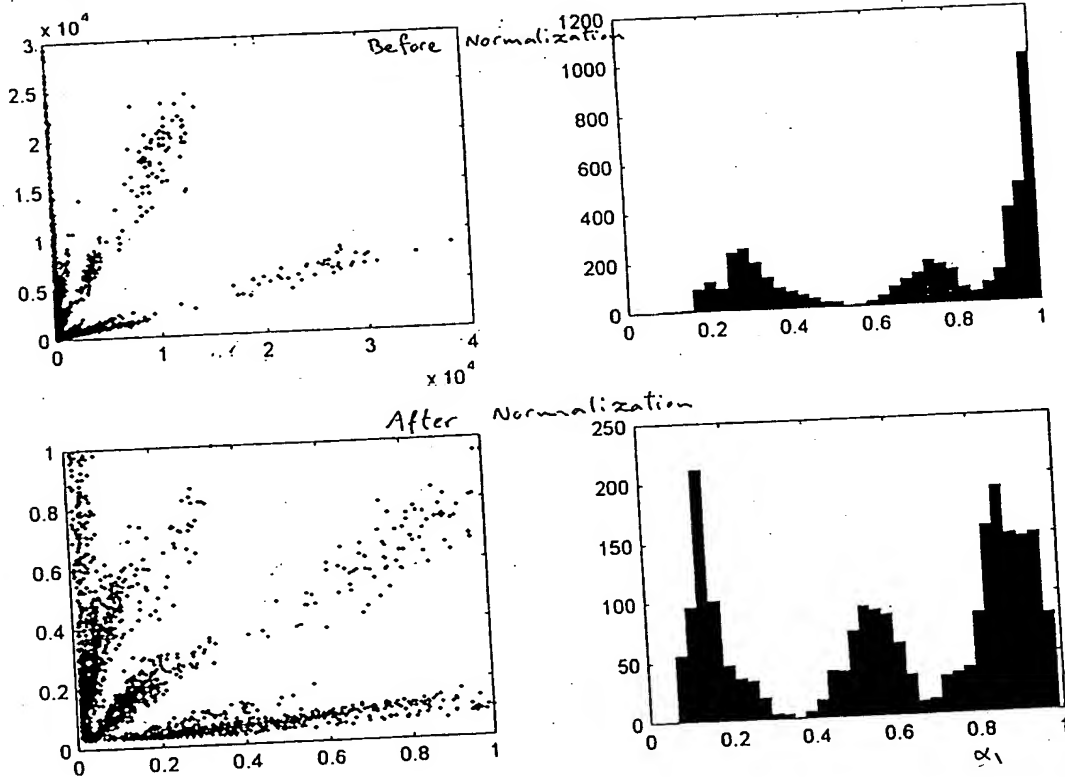


Figure 21

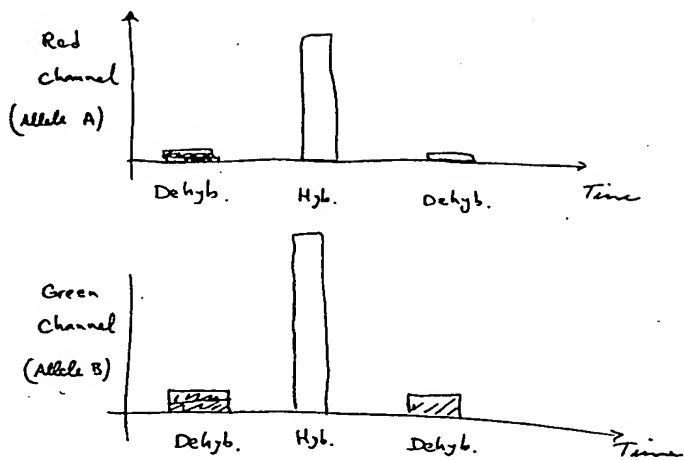


Fig. 21

A

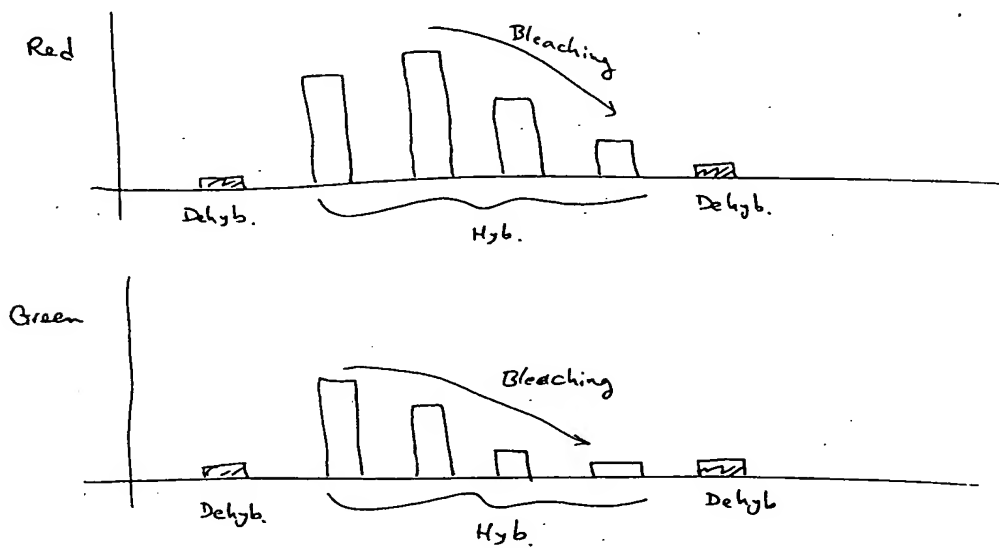


Fig. 22

B

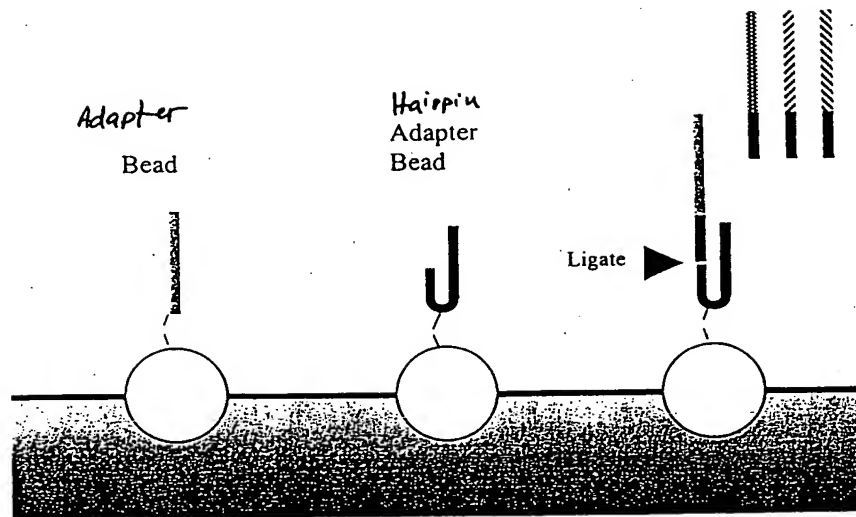
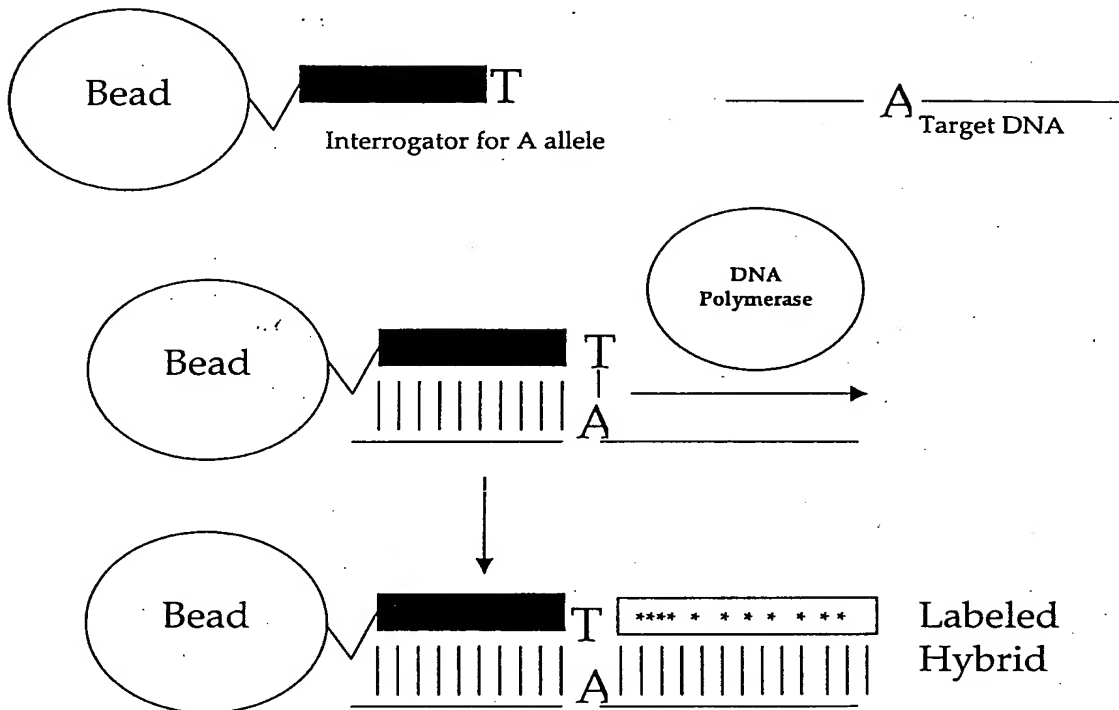


Figure 23

## A. Match to SNP allele



## B. Mismatch to SNP allele

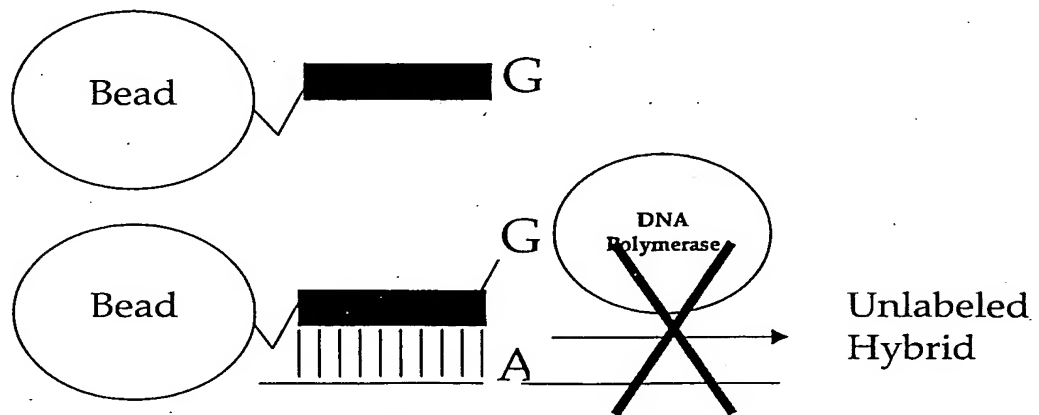
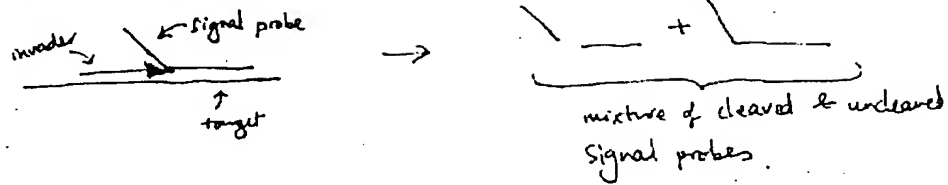


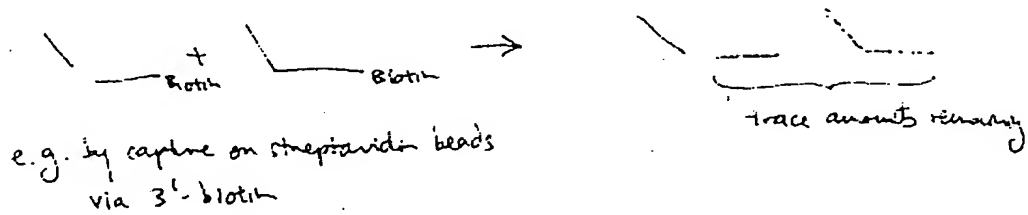
Figure 24

## Invader-PCR

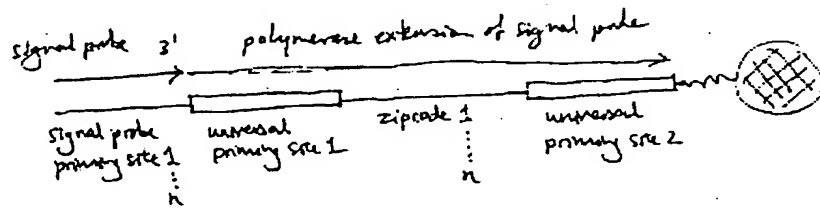
### 1) Invader reaction



### 2) Removal of uncleaved signal probes



### 3) Signal probe primes synthesis of amplicon target strand



### 4) PCR amplification

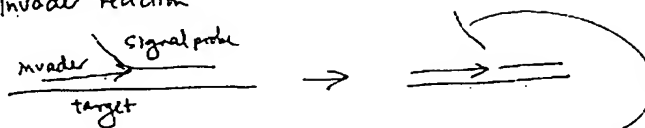
newly synthesized target strands are denatured from template & transferred to PCR reaction (universal primers, dNTPs, tag polymerase) for multiplex PCR. Universal primers are labelled e.g. with protein.

### 5) Array hybridization - PCR amplicons containing zipcodes are hybridized to array

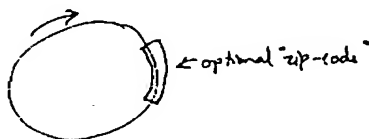
Figure 25

# Invader-Rolling Circle

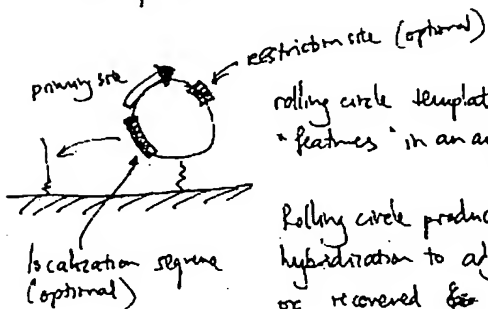
1) Invader reaction



... signal probe acts as primer on "rolling circle" template DNA



Solid-phase version:



rolling circle template is tethered to surface e.g. to localized "features" in an array format, or to beads.

Rolling circle products can be localized e.g. by hybridization to adjacent probes or recovered ~~for~~ in liquid phase for hybridization to a detection array. e.g. by enzymatic cleavage

Figure 26